

CLEAN COPY OF THE PENDING CLAIMS

12. A method for preparing a suppression effector and replacement nucleic acid, said method comprising:

a) preparing a suppression effector that binds to a coding region of a mature RNA encoding a mutant allele, thereby to inhibit the expression of the mutant allele; and

b) preparing a replacement nucleic acid that encodes a wild-type or non-disease causing allele and that comprises at least one degenerate / wobble nucleotide that is altered so that the replacement nucleic acid is not suppressed, or is only partially suppressed, by the suppression effector.

13. A method for preparing a suppression effector and replacement nucleic acid, the method comprising:

a) preparing a ribozyme that cleaves a mature RNA encoding a mutant; and

b) preparing a replacement nucleic acid that encodes a wild-type or non-disease causing allele and that comprises at least one degenerate / wobble nucleotide that is altered so that the replacement nucleic acid is not suppressed, or is only partially suppressed, by the ribozyme.

14. The method of claim 12, wherein the suppression effector is a nucleic acid or a peptide nucleic acid (PNA).

16. The method of claim 12, wherein the suppression effector is a nucleic acid that forms a triple helix with the mutant allele.

17. The method of claim 12, wherein the suppression effector is an nucleic acid.

18. The method of claim 12, wherein the suppression effector is a single-stranded RNA.

19. The method of claim 12, wherein the suppression effector is a ribozyme that cleaves an RNA encoded by the mutant allele.

20. The method of claim 19, wherein the ribozyme cleaves the RNA at an NUX ribozyme cleavage site.
21. The method of claim 12 or 13, wherein the suppression effector is operatively linked to an expression vector.
25. The method of claim 12 or 13, wherein the replacement nucleic acid encodes a protein selected from the group consisting of mammalian rhodopsin, collagen 1A1, collagen 1A2 and peripherin.
26. The method of claim 12 or 13, wherein the replacement nucleic acid is operatively linked to an expression vector.
27. The method of claim 21, wherein the expression vector is a viral expression vector.
30. The kit of claim 44, wherein the suppression effector is a nucleic acid or a peptide nucleic acid (PNA).
32. The kit of claim 44, wherein the suppression effector is a nucleic acid that forms a triple helix with the mutant allele.
33. The kit of claim 44, wherein the suppression effector is an nucleic acid.
34. The kit of claim 44, wherein the suppression effector is a single-stranded RNA.
35. The kit of claim 44, wherein the suppression effector is a ribozyme that cleaves an RNA encoded by the mutant allele.
36. The kit of claim 35, wherein the ribozyme cleaves the RNA at an NUX ribozyme cleavage site.
37. The kit of claim 44, wherein the suppression effector is operatively linked to an expression vector.
41. The kit of claim 44 or 45, wherein the replacement nucleic acid encodes a protein selected from the group consisting of mammalian rhodopsin, collagen 1A1, collagen 1A2 and peripherin.

42. The kit of claim 44 or 45, wherein the replacement nucleic acid is operatively linked to an expression vector.

43. The kit of claim 42, wherein the expression vector is a viral expression vector.

44. A kit comprising:

a suppression effector that suppresses the expression of a mature RNA encoding a mutant allele; and

a replacement nucleic acid that encodes a wild-type or non-disease causing allele that is not suppressed, or is only partially suppressed, by the suppression effector and that differs from the mutant allele in at least one degenerate / wobble nucleotide.

45. A kit comprising:

at least one ribozyme that cleaves a mature RNA encoding a mutant allele; and

a replacement nucleic acid that encodes a wild-type or non-disease causing allele and that is not suppressed, or is only partially suppressed, by the suppression effectors, wherein the replacement nucleic acid differs from the mutant allele in at least one degenerate / wobble nucleotide.

46. A ribozyme comprising nucleotides 101 - 137 of SEQ ID NO:4.

47. A ribozyme comprising nucleotides 116 - 153 of SEQ ID NO:14.

48. A ribozyme comprising nucleotides 112 - 148 of SEQ ID NO:15.

49. A ribozyme comprising nucleotides 107 - 141 of SEQ ID NO:18.

50. The method of claim 26, wherein the expression vector is a viral expression vector.

51. A therapeutic composition, the composition comprising:

a) a suppression effector that binds to the coding region of a mature RNA encoding a mutant allele, thereby to inhibit the expression of the mutant allele; and

b) a replacement nucleic acid that encodes a wild-type or non-disease causing allele and that comprises at least one degenerate / wobble nucleotide that is altered so that

the replacement nucleic acid is not suppressed, or is only partially suppressed, by the suppression effector.

52. A therapeutic composition, the composition comprising:

- a) a ribozyme that cleaves a mature RNA encoding a mutant allele; and
- b) a replacement nucleic acid that encodes a wild-type or non-disease causing allele and that comprises at least one degenerate / wobble nucleotide that is altered so that the replacement nucleic acid is not suppressed, or is only partially suppressed, by the ribozyme.

53. The composition of claim 51, wherein the suppression effector is a nucleic acid or a peptide nucleic acid (PNA).

54. The composition of claim 51, wherein the suppression effector is a nucleic acid that forms a triple helix with the mutant allele.

55. The composition of claim 51, wherein the suppression effector is an nucleic acid.

56. The composition of claim 51, wherein the suppression effector is a single-stranded RNA.

57. The composition of claim 51, wherein the suppression effector is a ribozyme that cleaves an RNA encoded by the mutant allele.

58. The composition of claim 57, wherein the ribozyme cleaves the RNA at an NUX ribozyme cleavage site.

59. The composition of claim 51, wherein the suppression effector is operatively linked to an expression vector.

60. The composition of claim 52, wherein the ribozyme is operatively linked to an expression vector.

61. The composition of claim 59 or 60, wherein the expression vector is a viral expression vector.

62. The composition of claim 51 or 52, wherein the replacement nucleic acid encodes a protein selected from the group consisting of mammalian rhodopsin, collagen 1A1, collagen 1A2 and peripherin.
63. The composition of claim 51 or 52, wherein the replacement nucleic acid is operatively linked to an expression vector.
64. The composition of claim 63, wherein the expression vector is a viral expression vector.
65. The composition of claim 52, wherein the ribozyme comprises a sequence selected from the group consisting of nucleotides 101 - 137 of SEQ ID NO:4, nucleotides 116 - 153 of SEQ ID NO:14, nucleotides 112 - 148 of SEQ ID NO:15, and nucleotides 107 - 141 of SEQ ID NO:18.
66. The method of claim 13, wherein the ribozyme comprises a sequence selected from the group consisting of nucleotides 101 - 137 of SEQ ID NO:4, nucleotides 116 - 153 of SEQ ID NO:14, nucleotides 112 - 148 of SEQ ID NO:15, and nucleotides 107 - 141 of SEQ ID NO:18.
67. The kit of claim 45, wherein the ribozyme comprises a sequence selected from the group consisting of nucleotides 101 - 137 of SEQ ID NO:4, nucleotides 116 - 153 of SEQ ID NO:14, nucleotides 112 - 148 of SEQ ID NO:15, and nucleotides 107 - 141 of SEQ ID NO:18.
68. The kit of claim 45, wherein the ribozyme is operatively linked to an expression vector.
69. The kit of claim 37 or 68, wherein the expression vector is a viral expression vector.
70. The method of claim 12 or 13, wherein the suppression effector suppresses both alleles of an endogenous gene.
71. The kit of claim 44, wherein the suppression effector suppresses both alleles of an endogenous gene.

72. The kit of claim 45, wherein the ribozyme suppresses both alleles of an endogenous gene.
73. The composition of claim 51, wherein the suppression effector suppresses both alleles of an endogenous gene.
74. The composition of claim 52, wherein the ribozyme suppresses both alleles of an endogenous gene.
75. The method of claim 12 or 13, wherein the RNA is an mRNA.
76. The kit of claim 44 or 45, wherein the RNA is an mRNA.
77. The composition of claim 51 or 52, wherein the RNA is an mRNA.